Stem cell differentiation to thymic epithelium for inducing tolerance to stem cells

Grant Award Details

Stem cell differentiation to thymic epithelium for inducing tolerance to stem cells

Grant Type: Transplantation Immunology

Grant Number: RM1-01702

Project Objective: The overall objective of this project is to generate functional thymic epithelial cells via the differentiation of hESC for the induction of immune tolerance

Investigator:

Name:	Mark Anderson
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: HIV/AIDS, Immune Disease, Infectious Disease, Pediatrics

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $1,314,089

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Stem cell differentiation to thymic epithelium for inducing tolerance to stem cells

Public Abstract: The thymus is an organ that plays a key role in controlling immune responses and immune tolerance. The thymus promotes immune tolerance by deleting and removing self-reactive T cells from the immune system. In addition, the thymus also helps drive the production of important suppressor T cell populations like regulatory T cells that also control immune tolerance. Thus, strategies that expand and improve thymic function could be critical in improving transplantation of tissues derived from embryonic stem cells. The thymus consists of a supporting network of thymic epithelial cells that help bone marrow derived T cell precursors mature and differentiate into fully functional T lymphocytes. Despite their importance, there has been little progress in methods to grow and expand out the supportive thymic epithelial network. This project will explore strategies to grow and expand out functional thymic epithelial cells from human embryonic stem cells using a multi-step culturing technique. These expanded thymic epithelial cells will be characterized and tested for the ability to support T cell development and differentiation. Finally, the expanded thymic epithelial cells will be put into transplantation models in humanized mice to test their ability to improve and enhance the acceptance of transplanted tissues. These studies offer enormous potential for promoting graft-specific immune tolerance in that embryonic stem cells could be differentiated into both a replacement tissue and into functional thymus

Statement of Benefit to California: The work in this proposal is designed to help improve the effectiveness of stem cell treatments by preventing immunological rejection of transplanted tissue derived from stem cells. Although significant progress and promise has been shown to use stem cells to regenerate damaged organs for the treatment of a wide variety of diseases, an important barrier to bringing this to the clinic is the potential of the immune system to reject or damage this regenerated tissue. Currently, there are efforts underway to use stem cells to treat diseases that have a wide impact on the health of Californians, including diabetes, Parkinson's disease, Alzheimer's disease, retinal eye diseases, and musculoskeletal diseases to name just a few.
The work proposed here will help improve treatment for these diseases by improving the ability to put a break on the immune system to reject or destroy cells or tissues that are derived from stem cells for the treatment of these diseases. Here we will improve methods to grow and expand an important organ that controls the ability of the immune system to be "tolerant" of transplanted tissues called the thymus. If methods to grow and expand the thymus from stem cells can be done, this would represent a significant advance in improving stem cell therapies. Thus, the impact of this work could have a broad impact on a large number of the disease treatments that involve stem cells.